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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/726,211	10/04/1996	MAR TORMO	UTXC:504	8827

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EXAMINER	
SULLIVAN, DANIEL M	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/726,211	TORMO ET AL.	
	Examiner	Art Unit	
	Daniel M Sullivan	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-15,18-20,22-25,28-30,44,46,58-65,72-76,79-89,91 and 92* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *11-15,18-20,44,88,89 and 91* is/are allowed.

6)☒ Claim(s) *22-25,28-30,46,58-65,72-76,79-87 and 92* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Non-Final Office Action is a response to the Paper filed 15 March 2004 in reply to the Non-Final Office Action mailed 12 December 2004. Claims 10-30, 44, 46 and 57-93 were considered in the 12 December Office Action. Claims 10, 16, 17, 21, 26, 27, 57, 66-71, 77, 78, 90 and 93 were canceled and claims 11, 13, 14, 18, 19, 22, 24, 28-30, 58, 59, 61, 63, 65, 72, 81, 85, 86, 88, 91 and 92 were amended in the 15 March Paper. Claims 11-15, 18-20, 22-25, 28-30, 44, 46, 58-65, 72-76, 79-89, 91 and 92 are pending and under consideration.

Response to Amendment

Objection to and rejection of claims 10, 16, 17, 21, 26, 27, 57, 66-71, 77, 78, 90 and 93 is rendered moot by cancellation of the claims.

Double Patenting

In the previous Office Action, it was noted that copending application 09/381,747 appears to disclose subject matter in common with this application and may recite the same or overlapping Inventions but, since 09/381,747 was not available for review, no determination was made as to whether or not a double patenting rejection should be applied to the claims of the instant application. The claims of the '747 application have now been considered and the instant claims are deemed patentably distinct therefrom.

Claim Rejections - 35 USC § 112

Rejection of claims 11-15, 18-20, 44, 88 and 91 under 35 U.S.C. 112, first paragraph, as lacking enablement for the full scope of the claims is withdrawn in view of the arguments set forth in the 15 March Paper.

Rejection of claims 28 and 30 under 35 U.S.C. §112, second paragraph, as indefinite in the recitation of "said composition" is withdrawn in view of the amendments thereto.

Claim 29 stands rejected and claims 22-25, 28, 30, 46 and 92 are newly rejected under 35 U.S.C. §112, second paragraph, as indefinite in the recitation of "said composition". There is still no antecedent basis for the limitation in the claim. Claims 22-25, 28, 30, 46 and 92 have been amended such that they now depend from claim 29 and are therefore now indefinite insofar as they depend from claim 29.

Rejection of claim 91 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements is withdrawn. Due to a typographical error, this rejection, which should have been applied to claim 93, was set forth against claim 91. As claim 93 has been canceled, the rejection is now moot.

Claim Rejections - 35 USC § 103

Rejection of claims 11-15, 18, 22-25, 28, 44, 46, 58-65, 72-76 and 79-85under 35 U.S.C. 103(a) as being unpatentable over Reed (WO/ 9508350) in view of Tari *et al.* (1995) U.S. Patent No. 5,417,978 is withdrawn.

The claims are now limited either to administering the composition at a dosage of about 5 to about 30 mg polynucleotide per m^2 or to a composition comprising both a neutral phospholipid and a charged phospholipid. With regard to the dosage limitation, assuming an average sized human of 150 cm and 70 kg, the Examiner has calculated an equivalent dosage of about 0.1 to about 0.7 mg polynucleotide per kg. The art of record teaches an effective dosage of 10-15 mg polynucleotide per kg in a SCID mouse xenotransplantation model (see Abubakr *et al.* *Blood* 10 suppl. 1:374A). Given the order of magnitude difference from the dosage described by Abubakr *et al.*, the dosage range recited in the claim would not have been obvious to one of ordinary skill in the art at the time of filing based on the available teachings.

With regard to the addition of a charged phospholipid to a neutral phospholipid composition, the art provides neither the instruction nor the motivation to so modify the teachings of record.

Rejection of claims 11-15, 18, 22-25, 28, 44, 46, 58-65, 72-76 and 79-85 under 35 U.S.C. 103(a) as being unpatentable over Tormo *et al.* (1996) *Proc. Am. Assoc. Cancer Res. Ann. Meeting* 37:173 in view of Tari *et al.* and in further view of Reed is withdrawn for the reasons set forth herein above regarding rejection of the claims as obvious over Reed in view of Tari.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 72, 79 and 80 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising an expression construct that encodes an oligonucleotide wherein said oligonucleotide hybridizes to Bcl-2 mRNA under intracellular conditions, does not reasonably provide enablement for a composition comprising an expression construct that encodes any oligonucleotide of from about 8 to 50 bases and complementary to at least 8 bases of the translation initiation site of Bcl-2 mRNA. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The previous Office Action sets forth a *prima facie* case as to why the disclosure fails to teach the skilled artisan how to use compositions broadly encompassing any nucleic acid comprising 8 bases of the translation initiation site of Bcl-2 mRNA (see especially the discussion beginning the first full paragraph on page 3 and continued through the first paragraph on page 8). Briefly, the Office Action argues that because each of the four nucleotides found in naturally occurring nucleic acids appear at least twice in the translation initiation site of the Bcl-2 mRNA, a nucleic acid limited to comprising 8 bases complementary to the translation initiation site of Bcl-2 mRNA, wherein the order of the nucleotide sequence is not limited to being the same as the order found in the Bcl-2 translation initiation site, encompasses essentially any nucleic acid.

In the 15 March response, Applicant argues persuasively that the disclosure is enabling for antisense molecules that hybridize to any portion of the Bcl-2 mRNA under intracellular conditions. However, upon further consideration it is clear that claims 72, 79 and 80 are not limited to this enabled scope. The claims are directed to a composition comprising an expression construct that encodes an oligonucleotide of from about 8 to 50 bases and complementary to at least 8 bases of the translation initiation site of Bcl-2 mRNA. Thus, the oligonucleotide of the claims might comprise any sequence of nucleotides found in the translation initiation site of Bcl-2 mRNA (*i.e.*, A, G, C or T). Thus, for the reasons set forth in the previous Office Action and herein, the instant disclosure is not enabling for the full scope of the subject matter of claims 72, 79 and 80.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 58-65, 72-76 and 79-87 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 65, 72, 81 and 86 have been amended such that they are now limited to a composition and method of using a composition comprising a nucleic acid associated with a neutral phospholipid and further comprising a charged phospholipid. However, claims 76, 80, 83 and 74, which depend from claims 65, 72, 81 and 86, respectively, limit the lipid to consisting essentially of neutral lipids. Given that the Office understands the "consisting essentially of" transition to limit the scope of the claim to the recited element and those that do not materially

affect the basic and novel characteristics of the invention, it is unclear how the scope of the composition containing both a neutral and charged phospholipid should be interpreted. For example, do the claims include embodiments wherein the concentration of charged phospholipid is so low that it does not affect the basic and novel characteristics of the invention? If so, then the art would still apply because the charged phospholipid would not contribute to the novel characteristics. In other words, the composition containing the charged phospholipid is understood to be essentially the same as the composition that does not contain a charged phospholipid, and is therefore anticipated by the composition comprising the neutral phospholipid alone. On the other hand, if the presence of the charged phospholipid is to be taken as relevant to the basic and novel aspects of the claims, then limitation to consisting essentially of neutral lipids is outside of the scope of the base claim. Clarification is requested.

Claim 73 is additionally indefinite as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: those elements recited in the base claim 57. Claim 57 is now canceled.

Allowable Subject Matter

Claims 11-15, 18-20, 44, 88, 89 and 91 are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel M Sullivan whose telephone number is 571-272-0779. The examiner can normally be reached on Monday through Thursday 6:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DMS

DAVID GUZO
PRIMARY EXAMINER